**ABSTRACT**

The invention relates to a method for marker-free repetitive DNA expression cassette exchange in the genome of cells or parts of cells by using the FLP recombinase mediated cassette exchange. In a first step a first DNA expression cassette carrying a positive-negative selection marker flanked by a wild type FLP recombinase recognition target (FRT) site on one end and a modified heterospecific FRT on the other end is integrated into a chromosomal locus of the genome for tagging. Following selection of cell clones surviving the conditions for positive selection said first DNA cassette as a second step is exchanged by an incoming second DNA expression cassette located on a circular vector and carrying a homologous or heterologous gene (transgene) of any coding sequence flanked by the same FRT sites as the first DNA cassette by using FLP-recombinase. The cell clones surviving the conditions for negative selection contain specifically inserted the gene of the incoming DNA cassette without inserted unwanted vector sequences or positive selectable markers.